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The presence of a mutation in a tumor suppressor gene, such as BRCA1, may have implications for patient management if patients with these mutations can be identified. Specifically, treatments such as breast conserving surgery and radiation therapy may be inappropriate if these patients are likely to be more susceptible to radiation-induced carcinogenesis or if they are more likely to recur locally in the breast because of multicentric disease. We have to date identified 189 eligible patients diagnosed with breast cancer at age 38 or younger and treated at the Joint Center for Radiation Therapy (JCRT) between 1987-95 of the 226 whom we expect to eventually contact. Patient accrual is steady and ongoing with 39 patients accrued to date. Lymphocytes from study subjects are being collected, immortalized and stored in liquid nitrogen. At the end of the two year collection period, testing for the presence of a germ-line BRCA1 mutation will be performed. Treatment outcome will then be compared between the groups of patients with and without mutations in BRCA1. In addition we have begun identifying our "on treatment cohort" of patients currently undergoing radiation therapy, and plan to begin enrolling this group early next month.

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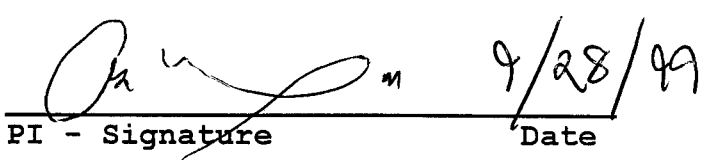

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INTRODUCTION:

The presence of a germ line mutation in a tumor suppressor gene, such as BRCA1, may have implications for patient management if patients with these mutations can be identified. Specifically, treatments such as breast conserving surgery and radiation therapy may be inappropriate if these patients are likely to be more susceptible to radiation-induced carcinogenesis or if they are more likely to recur locally in the breast because of multicentric disease. This study will investigate the treatment outcomes after conservative surgery and radiation therapy among a cohort of young breast cancer patients who have BRCA1 mutations and a similarly-aged group who do not have mutations in BRCA1. The blood of young patients diagnosed with early-stage invasive breast cancer will be drawn and tested for the presence of mutations in the tumor suppressor gene BRCA1. At the end of three years, treatment outcomes will be compared between the patients in this group who have a mutation in the BRCA1 gene and those patients who do not. Blood will also be stored in order to test for mutations in other breast cancer susceptibility genes as such genes are identified and testing becomes available. A second objective will be to determine patient preferences regarding the optimal time to consider genetic testing for breast cancer susceptibility genes in this patient population. Since the results of testing may influence local treatment decisions, patient preferences for the timing of testing assume added importance.

BODY:

Methods: We have to date identified 189 eligible patients diagnosed with breast cancer at age 38 or younger and treated at the Joint Center for Radiation Therapy at Harvard Medical School between 1987-95 of the 226 whom we expect to eventually contact. We have also decided to add another year's worth of patients (1996) in order to increase our population size. By extending the treatment years, we estimate that we will have an additional 25 patients whom we can contact.

The blood collection protocol has been altered from the initial proposal such that we now intend to immortalize lymphocytes from each patient's blood sample to allow for adequate supplies of DNA to permit testing for other gene mutations (such as BRCA2) [1]. Once transformed, aliquots of these cells will be frozen for later BRCA1 testing as specified in the original protocol. To date, 39 patients have been accrued. This process is being ramped up with an increase in the number of letters sent out to patients per month. We have also begun identifying our "on treatment cohort" of patients who are currently undergoing radiation therapy. We plan to begin enrolling this group early next month.

Results: See above. No data has yet been generated from this study. There are currently no negative nor positive findings related to this project.

Progress related to statement-of-work:

Task 1	Months 1-6	Completed
Task 2	Months 1-6	Completed
Task 3	Months 3-24	In progress
Task 4	Months 6-24	Initiated
Task 5	Months 6-30	In progress
Task 6	Months 6-36	In progress
Task 7	Months 24-34	Not yet initiated
Task 8	Months 30-33	Not yet initiated
Task 9	Months 33-36	Not yet initiated

KEY RESEARCH ACCOMPLISHMENTS: None to date, pending analysis.

REPORTABLE OUTCOMES:

-cell lines for 27 of the 39 accrued patients have been successfully immortalized and stored in liquid nitrogen.

CONCLUSIONS:

Currently we are on target to collect blood specimens for DNA analysis on all eligible patients. There are currently no positive nor negative findings from this project.

REFERENCES:

1. M. A. Anderson and J. F. Gusella, *In Vitro* **20**, 856 (1984).